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Chapter 38: Gastrointestinal Infections

INTRODUCTION

- Definition: Gastrointestinal (GI) infections encompass a wide variety of medical conditions characterized by inflammation of the GI tract.
- Dehydration resulting from *GI infections* such as acute infectious diarrhea is the second leading cause of mortality in children younger than 5 years, killing 443,000 annually. Globally, 1.7 billion cases of infectious diarrhea occur yearly and cause over 1.39 million deaths.
- Viruses are now the leading global cause of infectious diarrhea. Noroviruses account for greater than 90% of viral gastroenteritis among all age groups and 50% of outbreaks worldwide. Characteristics of agents responsible for viral gastroenteritis are given in **Table 38-1**.
- Public health measures such as clean water supply and sanitation facilities, as well as quality control of commercial products, are important for the control of most enteric infections. Sanitary food handling and preparation practices significantly decrease the incidence of enteric infections.
- Common pathogens responsible for watery diarrhea in the United States are norovirus and enterotoxigenic *Escherichia coli* (ETEC), while those most commonly associated bacteria with dysentery diarrhea are *Campylobacter* spp., enterohemorrhagic *E. coli* (EHEC), *Salmonella* spp., and *Shigella* spp. (**Table 38-2**). ETEC is also the most common cause of traveler's diarrhea and a common cause of food- and water-associated outbreaks. Cholera is caused by toxigenic *Vibrio cholerae*.

TABLE 38-1

Characteristics of Agents Responsible for Acute Viral Gastroenteritis

Virus	Peak Age of Onset	Time of Year	Duration	Mode of Transmission	Common Symptoms
Rotavirus	6 months to 2 years	October to April	3–7 days	Fecal–oral, water, food	Nausea, vomiting, diarrhea, fever, abdominal pain, lactose intolerance
Norovirus	All age groups	Peak in winter	2–3 days	Fecal–oral, food, water, environment	Nausea, vomiting, diarrhea, abdominal cramps, myalgia
Astrovirus	<7 years	Winter	1–4 days	Fecal–oral, water, shellfish	Diarrhea, headache, malaise, nausea
Enteric adenovirus	<2 years	Year-round	7–9 days	Fecal–oral	Diarrhea, respiratory symptoms, vomiting, fever
Pestivirus	<2 years	NR	3 days	NR	Mild
Coronavirus-like particles	<2 years	Fall and early winter	7 days	NR	Respiratory disease
Enterovirus	NR	NR	NR	NR	Mild diarrhea, secondary organ damage

NR, not reported.

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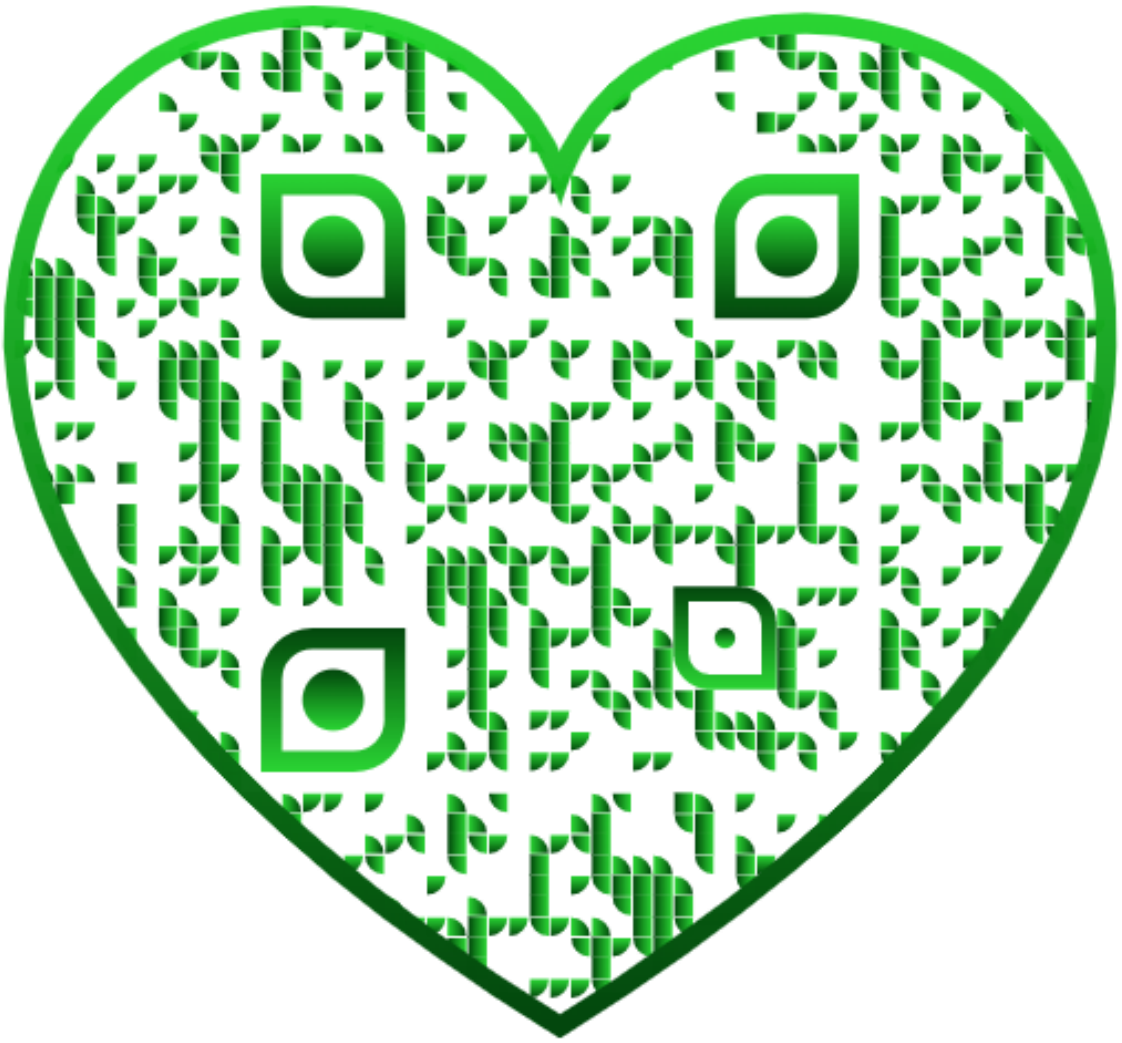

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TABLE 38-2

Characteristics of Acute Bacterial Gastroenteritis

Bacteria	Incubation Period	Duration	Mode of Transmission	Common Symptoms
Watery Diarrhea				
V. cholerae	2–3 days	1–3 days	Contaminated food or water with human feces usually in areas of inadequate treatment of sewage and drinking water	Profuse watery diarrhea, vomiting, and leg cramps Death can occur within hours without treatment
Enteroaggregative *E. coli*	NR	NR	Contaminated food or water with animal or human feces	Chronic, watery, mucoid, secretory diarrhea with low-grade fever in immunocompromised persons (HIV infections)
Enteroinvasive *E. coli*	10–18 hours	NR	Contaminated food or water with animal or human feces	Watery diarrhea in young children in the developing world
Enteropathogenic *E. coli*	9–12 hours	NR	Contaminated food or water with animal or human feces	Acute onset of profuse watery diarrhea, vomiting, and low-grade fever in young children (<2 years of age) in the developing world
Enterotoxigenic *E. coli*	1–3 days	3–4 days	Contaminated food or water with animal or human feces	Watery diarrhea and abdominal cramping
Dysentery Diarrhea				
Campylobacter jejuni	2–5 days	5–7 days	Contaminated food (particularly poultry), water, or contact with infected animals	Diarrhea (often bloody), cramping, abdominal pain, and fever
Enterohemorrhagic *E. coli*	3–4 days	5–7 days	Contaminated food (particularly cattle) or water with animal or human feces	Severe stomach cramps, diarrhea (often bloody), and vomiting
				Approximately 5%–10% develop hemolytic uremic syndrome
Nontyphoid *Salmonella*	12–36 hours	1–5 days	Contaminated food, water, or contact with infected animals	Diarrhea (sometimes bloody), fever, and abdominal cramps
Shigella	1–3 days	1–7 days	Fecal–oral Contaminated food or water with infected human feces	Watery or bloody diarrhea (8–10 stools/day), severe abdominal pain, fever, and malaise
Yersinia	4–7 days	1–3 weeks	Contaminated food or water	Fever, abdominal pain, and diarrhea (often bloody)

NR, not reported.

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REHYDRATION, ANTIMOTILITY, AND PROBIOTIC THERAPY

- The cornerstone of management for all GI infections and enterotoxigenic poisonings is to prevent dehydration by correcting fluid and electrolyte imbalances. In mild, self-limiting acute gastroenteritis, a diet of oral fluids and easily digestible foods is recommended. In patients with severe dehydrating watery diarrhea and dysenteric diarrhea, intravenous (IV) rehydration therapy, antibiotics, and/or antimotility treatments are needed.
- Initial assessment of fluid loss is essential for successful rehydration therapy and should include acute weight loss, as it is the most reliable means of determining the extent of water loss. Clinical signs can be helpful in determining approximate deficits (**Table 38-3**).
- The necessary components of **oral rehydration solution** (ORS) include glucose, sodium, potassium chloride, and water (**Table 38-4**). ORS should be given in small frequent volumes (5 mL every 2–3 minutes) in a teaspoon or oral syringe.
- Severely dehydrated patients should be resuscitated initially with lactated Ringer's solution or normal IV saline. Guidelines for rehydration therapy based on the degree of dehydration and replacement of ongoing losses are outlined in **Table 38-3**. After rehydration, maintenance fluid is given based on accurate recording of intake and output volumes. ORS should be instituted as soon as it can be tolerated.
- Early refeeding with age-appropriate unrestricted diet is recommended in children and shortens the course of diarrhea. Initially, easily digested foods, such as bananas, applesauce, and cereal may be added as tolerated. Foods high in fiber, sodium, and sugar should be avoided.
- Antimotility drugs such as **diphenoxylate** and **loperamide** offer symptomatic relief in patients with watery diarrhea by reducing the number of stools. Antimotility drugs should be avoided if possible and are not recommended in patients with many toxin-mediated dysenteric diarrheas (ie, EHEC, pseudomembranous colitis, shigellosis).
- Individual studies have not shown significant benefit from probiotics, and meta-analyses have shown conflicting results.
- Oral zinc supplementation of 20 mg/day for 1–2 weeks may have an additional benefit over ORS alone in reducing childhood mortality in developing countries.

TABLE 38-3

Clinical Assessment of Degree of Dehydration in Children Based on Percentage of Body Weight Loss[a]

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Variable	Minimal or No Dehydration (<3% Loss of Body Weight)	Mild-to-Moderate (3%–9% Loss of Body Weight)	Severe (≥10% Loss of Body Weight)
Blood pressure	Normal	Normal	Normal to reduced
Quality of pulses	Normal	Normal or slightly decreased	Weak, thready, or not palpable
Heart rate	Normal	Normal to increased	Increased (bradycardia in severe cases)
Breathing	Normal	Normal to fast	Deep
Mental status	Normal	Normal to listless	Apathetic, lethargic, or comatose
Eyes	Normal	Sunken orbits/decreased tears	Deeply sunken orbits/absent tears
Mouth and tongue	Moist	Dry	Parched
Thirst	Normal	Eager to drink	Drinks poorly; too lethargic to drink
Skin fold	Normal	Recoil in <2 seconds	Recoil in >2 seconds
Extremities	Warm, normal capillary refill	Cool, prolonged capillary refill	Cold, mottled, cyanotic, prolonged capillary refill
Urine output	Normal to decreased	Decreased	Minimal
Hydration therapy	None	ORS 50–100 mL/kg over 3–4 hours	Lactated Ringer's solution or normal saline 20 mL/kg over 15–30 minutes IV until mental status or perfusion improves Followed by 5% dextrose/0.45% sodium chloride IV at higher maintenance rates or ORS 100 mL/kg over 4 hours
Replacement of ongoing losses	For each diarrheal stool or emesis <10 kg body weight: 60–120 mL ORS >10 kg body weight: 120–240 mL ORS	Same as minimal dehydration	If unable to tolerate ORS, administer through nasogastric tube or administer 5% dextrose/0.45% sodium chloride with 20 mEq/L (mmol/L) potassium chloride IV

IV, intravenous; ORS, oral rehydration solution.

[a]Percentages vary among patients for each dehydration category; hemodynamic and perfusion status is most important; when unsure of category, therapy for more severe category is recommended.

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TABLE 38-4

Comparison of Common Solutions Used in Oral Rehydration and Maintenance

Product	Na (mEq/L)[a]	K (mEq/L)[a]	Base (mEq/L)	Carbohydrate (mmol/L)	Osmolarity (mOsm/L)
WHO/UNICEF (2002)	75	20	30	75	245
Pedialyte	45	20	30	140	250
Enfalyte	50	25	30	70	200
Oralyte	60	20	0	90	260
Rehydralyte	75	20	30	140	250
Cola[b]	2	0	13	700	750
Apple juice[b]	5	32	0	690	730
Chicken broth[b]	250	8	0	0	500
Sports beverage[b]	20	3	3	255	330

[a]Concentration of monovalent ions expressed in mEq/L is numerically equivalent to mmol/L concentration.

[b]These solutions should be avoided in dehydration.

BACTERIAL INFECTIONS

- Antibiotic therapy is recommended in severe cases of diarrhea, moderate-to-severe cases of traveler's diarrhea, most cases of febrile dysenteric diarrhea, and culture-proven bacterial diarrhea. Antimicrobial therapy is not recommended in EHEC diarrhea as it may increase risk of hemolytic uremic syndrome; however, it is recommended in severe cases of cholera and ETEC diarrhea. Antibiotic choices for bacterial infections are given in **Table 38-5**.
- Antibiotic therapy is indicated in at-risk and febrile patients with dysenteric diarrhea. In shigellosis, antibiotics shorten the period of fecal shedding and attenuate the clinical illness. Antibiotic therapy is reserved for the elderly, those who are immunocompromised, children in daycare centers, malnourished children, and healthcare workers.

TABLE 38-5

Recommendations for Antibiotic Therapy

Pathogen	Children	Adults
Watery Diarrhea		
Enterotoxigenic *Escherichia coli*	Azithromycin 10 mg/kg/day given orally once daily × 3 days; ceftriaxone 50 mg/kg/day given	Ciprofloxacin 750 mg orally once daily × 1–3 days; alternatives: rifaximin 200 mg orally three times daily × 3 days; azithromycin 1000 mg orally × 1 day *or* 500 mg orally daily × 3 days

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	IV once daily × 3 days	
Vibrio cholerae O1	Erythromycin 30 mg/kg/day divided every 8 hours orally × 3 days; azithromycin 10 mg/kg/day given orally once daily × 3 days	Doxycycline 300 mg orally × 1 day Alternatives: azithromycin 500 mg orally once daily × 3 days; ciprofloxacin 750 mg orally once daily × 3 days; ceftriaxone IV
Dysenteric Diarrhea		
Campylobacter species[a]	Azithromycin 10 mg/kg/day given orally once daily × 3–5 days; erythromycin 30 mg/kg/day divided into two to four doses orally × 3–5 days	Azithromycin 500 mg orally once daily × 3 days Alternatives: ciprofloxacin 750 mg orally once daily × 7 days
Salmonella Nontyphoidal[a]	Ceftriaxone 100 mg/kg/day divided IV every 12 hours × 7–10 days; azithromycin 20 mg/kg/day orally once daily × 7 days	Ceftriaxone 2 g IV/IM once; ciprofloxacin 750 mg orally once daily × 7–10 days Alternatives: ampicillin 250–500 mg orally every 6 hours × 7 days; azithromycin 500 mg orally once daily × 7 days; trimethoprim-sulfamethoxazole 160/800 mg twice daily × 7 days For immunocompromised patients, duration should be increased to 14 days for both fluoroquinolones and azithromycin
Shigella species[a]	Azithromycin 10 mg/kg/day given orally once daily × 3 days; ceftriaxone 50 mg/kg/day given IV once daily × 3 days	Azithromycin 500 mg orally once daily × 3 days; ceftriaxone 2 g IV/IM once; ciprofloxacin 750 mg orally once daily × 3 days Alternatives: ampicillin 250–500 mg orally every 6 hours × 7 days; trimethoprim–sulfamethoxazole 160/800 mg twice daily × 7 days
Yersinia species[a]	Treat as children with shigellosis	Trimethoprim-sulfamethoxazole 160/800 mg twice daily × 7 days Alternatives: cefotaxime IV or ciprofloxacin 750 mg orally once daily × 7 days
Traveler's Diarrhea		
Prophylaxis[a]		None recommended
Treatment		Azithromycin 1000 mg orally × 1 day or 500 mg orally daily × 3 days; ciprofloxacin 750 mg orally × 1 day or 500 mg orally every 12 hours × 3 days; levofloxacin 500 mg orally daily × 3 days; ofloxacin 400 mg twice daily × 1–3 days; rifamycin SV 388 mg twice daily × 3 days; rifaximin 200 mg three times daily × 3 days

[a]For high-risk patients only. See the preceding text for the high-risk patients in each infection.

TRAVELER'S DIARRHEA

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- Traveler's diarrhea describes the clinical syndrome caused by contaminated food or water that is manifested by malaise, anorexia, and abdominal cramps followed by the sudden onset of diarrhea that incapacitates many travelers.
- Traveler's diarrhea is caused by contaminated food or water. The most common pathogens are bacterial and include ETEC, *Campylobacter* spp., *Shigella* spp., and *Salmonella* spp.
- Patient education in avoiding high-risk food and beverages should be the best method for minimizing the risk. High-risk foods and beverages include raw or undercooked meat and seafood, moist foods served at room temperature, fruits that cannot be peeled, vegetables, milk from a questionable source, hot sauces on the table, tap water, unsealed bottled water, iced drinks, and food from street vendors.
- **Bismuth subsalicylate** 524 mg (two chewable tablets or 2 ounces) orally four times daily for up to 3 weeks is a commonly recommended prophylactic regimen. Prophylactic antibiotic use is not recommended for most travelers due to the potential side effects of antibiotics, predisposition to other infections such as *Clostridioides difficile* infection (CDI) or vaginal candidiasis, the increased risk of selection of drug-resistant organisms, cost, lack of data on the safety and efficacy of antibiotics given for more than 2 or 3 weeks, and availability of rapidly effective antibiotics for treatment.
- Prophylactic antibiotics are recommended only in high-risk individuals or in situations in which short-term illness could ruin the purpose of the trip, such as a military mission. A fluoroquinolone is the drug of choice when traveling to most areas of the world. **Azithromycin** can be considered when traveling to South and Southeast Asia. **Rifaximin** 200 mg once, twice, or three times daily with meals for 2 weeks should be reserved for travel regions where *E. coli* predominates, such as Latin America and Africa.

Treatment

- The goals of treatment of traveler's diarrhea are to avoid dehydration, reduce the severity and duration of symptoms, and prevent interruption to planned activities.
- Fluid and electrolyte replacement should be initiated at the onset of diarrhea. ORS is generally not required in otherwise healthy individuals; flavored mineral water offers a good source of sodium and glucose. In infants and young children, elderly, and those with chronic debilitating medical conditions, ORS is recommended.
- Antibiotics used for treatment are given in **Table 38-5**. A single dose of fluoroquinolone is recommended initially, and if diarrhea is improved within 12–24 hours, antibiotics should be discontinued.
- For symptom relief, **loperamide** (preferred because of its quicker onset and longer duration of relief relative to bismuth) may be taken (4 mg orally initially and then 2 mg with each subsequent loose stool to a maximum of 16 mg/day in patients without bloody diarrhea and fever). Loperamide should be discontinued if symptoms persist for more than 48 hours.

CLOSTRIDIOIDES DIFFICILE

- *C. difficile* is the most commonly recognized cause of infectious diarrhea in healthcare settings, with high rates of disease in the elderly and those exposed to antibiotic agents. The antibiotics most commonly associated with CDI include fluoroquinolones, clindamycin, carbapenems, and third-/fourth-generation cephalosporins.
- Other risk factors for acquisition of *C. difficile* include recent healthcare exposure, chemotherapy, patients undergoing GI surgery or receiving tube feeding, and potentially those receiving acid-suppressive medications.
- The spectrum of disease ranges from mild diarrhea to fulminant disease and toxic megacolon. The diarrhea is typically watery and nonbloody, and is often associated with abdominal discomfort, fever, and leukocytosis.
- Diagnosis of CDI is confirmed by identification of *C. difficile* organisms/toxin in stool or by colonoscopic or histopathologic findings revealing pseudomembranous colitis.
- Supportive care of CDI includes fluid and electrolyte replacement therapy, in addition to discontinuation of the offending antimicrobial if

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possible.

- Once determination of disease severity has been made, treatment should be initiated with an antibiotic effective against *C. difficile*. **Vancomycin** and **fidaxomicin** are the most commonly prescribed agents and fidaxomicin is the preferred therapy. The recommended treatment course is 10 days and repeat stool testing is not recommended as a test of cure. The patient should be supported with fluid and electrolyte replacement and discontinuation of the offending antimicrobial if possible.
- IDSA/SHEA 2021 clinical practice guidelines prefer fidaxomicin for initial CDI episodes based on emerging data demonstrating the sustained response and safety profile of fidaxomicin.
- Antimotility agents (such as **diphenoxylate/atropine** and loperamide) and exchange resins (such as **cholestyramine** and **colestipol**) have been used in CDI; however, their use is discouraged.
- Classification of CDI severity and recommended treatment for adults is given in **Table 38-6**. In patients with severe/complicated or fulminant CDI, the preferred regimen is combination therapy with IV **metronidazole** and **vancomycin**.
- Recurrence of CDI can occur in 15%–35% of patients. The preferred regimen for the first episode of recurrent CDI (rCDI) is fidaxomicin standard dose or an extended-pulsed regimen (200 mg twice daily for 5 days, then once every other day for 20 days). If metronidazole was used initially, then a standard vancomycin course can be utilized for the first recurrence. For patients with multiple recurrences, fidaxomicin remains the preferred agent; however, pulsed/tapered vancomycin, vancomycin followed by rifaximin, and fecal microbiota transplantation (FMT) are acceptable alternatives.
- FMT may be used for refractory fulminant CDI and rCDI.
- Live biotherapeutic products (**Rebyota** and **Vowst**) may be used for prevention of rCDI only after completion of a course of standard-of-care antibiotics for CDI treatment and a sufficient washout period.
- For patients with rCDI within 6 months, **bezlotoxumab** (10 mg/kg IV as a single dose during antibacterial treatment) may be used during the administration of standard-of-care antibiotics.

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TABLE 38-6

***Clostridioides difficile* Infection Severity and Treatment**

Severity	Markers of Disease Severity	Recommended Treatment
Nonsevere	WBC ≤15,000 cells/mm^3 (15×10^9/L) SCr <1.5 mg/dL (133 µmol/L)	Vancomycin 125 mg orally 4 times daily for 10 days, OR fidaxomicin 200 mg orally twice daily for 10 days, OR metronidazole 500 mg orally every 8 hours for 10 days[a]
Severe	WBC >15,000 cells/mm^3 (15×10^9/L) SCr >1.5 mg/dL (133 µmol/L)	Vancomycin 125 mg orally 4 times daily for 10 days, OR fidaxomicin 200 mg orally twice daily for 10 days
Fulminant	Hypotension or shock Ileus and/or megacolon	Metronidazole 500 mg IV every 8 hours *PLUS* vancomycin 500 mg every 6 hours via NG or orally (if ileus present use rectally)

NG, nasogastric; SCr, serum creatinine; WBC, white blood cell.

[a]Metronidazole is an alternative therapy if other agents are unavailable or too costly.

See Chapter 141, Gastrointestinal Infections and Enterotoxigenic Poisonings, authored by Andrew M. Roecker and Brittany N. Bates, for a more detailed discussion of this topic.

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